Editorial

Functional, Ischemic Mitral Regurgitation
To Repair or Not to Repair?

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With an ever increasing population of patients with coronary artery disease complicated by chronic ischemic mitral regurgitation (IMR), the question of whether to perform mitral valve repair (MVRep) in addition to coronary artery bypass grafting (CABG) is one of the most common and controversial clinical dilemmas faced by cardiac surgeons today. At present, there is no definitive randomized, prospective trial that clarifies exactly what approach should be taken.

The existing body of mostly retrospective and scant prospective literature is highly conflicting as a whole. Authors advocating MVRep cite the well-established negative impact that IMR has on survival in patients undergoing CABG alone,1 for whom the presence of even mild degrees of IMR is thought to increase long-term mortality. Retrospective data from our own institution suggest that adjunctive MVRep improves ventricular function, medium-term symptomatology, and survival in patients with IMR and poor ventricular function.2

Meanwhile, clinicians on the opposing view argue that because IMR is the result of an ischemic, maladaptively remodeled left ventricle (LV) in the setting of normal mitral valve leaflets, CABG alone should theoretically reverse the IMR by improving regional wall motion abnormalities, papillary muscle function, and stimulation of reverse LV remodeling3 without subjecting patients to the incremental perioperative morbidity and mortality with which adjunctive MVRep has been historically associated. Not surprisingly, however, whereas some retrospective studies show that CABG alone improves both IMR and functional status in the short term,4,5 others show that IMR is not reversed6 and may progress further,7 with attendant negative impact on survival.6

Further clouding the issue are the conflicting conclusions of animal and laboratory studies. Although some groups show that acute reversal of a volume-overloaded ovine model of IMR leads to significant reverse remodeling,8 others show just the opposite9 and suggest that IMR is more an effect and not an ongoing cause of the progressive LV remodeling that led to the development of IMR in the first place.

Given such mixed messages, is it any wonder that there is no current standard of care for surgeons when faced with IMR in the operating room? The decision to perform MVRep in addition to CABG is currently not guided by any clear and consistent finding in the literature but rather by a combination of tentatively formed regional guidelines, institutional practice patterns, and clinical gestalt gleaned from anecdotal evidence and a variety of clinical factors of ill-defined significance.

In this issue of Circulation, Deja and colleagues10 provide a timely and comprehensive survival analysis of 1212 patients enrolled in the Surgical Treatment for Ischemic Heart Failure (STICH) trial, focusing on the impact of (1) baseline severity of IMR in the overall cohort, and (2) the addition of concomitant adjunctive MVRep in a subset of patients with moderate-to-severe chronic IMR prospectively randomized by study design to receive CABG or optimized medical therapy. This study aptly hones in on the exact group of patients for whom the decision to perform MVRep is the most controversial: those with chronic mitral regurgitation (MR) secondary to chronic ischemia. Neither the coronary ischemia nor valvular insufficiency was acute.

As expected, higher IMR severity was associated with higher LV end-systolic volume index, lower LV ejection fraction, higher New York Heart Association heart failure class, and, most importantly, reduced long-term survival in the entire population overall as well as in both CABG and medical therapy patients separately by group. The sicker and larger the ventricle, the worse the IMR and long-term survival. No surprise here.

The key finding of this study, which stands in contrast to previous reports,11–13 is that patients with moderate to severe IMR who underwent MVRep in addition to CABG had lower 30-day mortality and improved long-term survival compared with (1) those who did not undergo MVRep and (2) corresponding patients in the medical therapy group. The authors conclude that for patients meeting the inclusion/exclusion criteria (coronary artery disease amenable to but not requiring CABG, LV ejection fraction ≥35%, Canadian Cardiovascular Society angina class ≥2, no need for aortic valve procedures, and no recent myocardial infarction), the addition of MVRep may improve early and long-term survival compared with CABG or medical therapy alone.

Why should this be so? In other words, why should eliminating MR overcome and trump the added operative complexity and risk of valve repair in general, to the point that it increases not only long-term survival but also decreases operative mortality by the addition of more surgery?
Patients in the CABG plus MVR group had more advanced LV disease, as evidenced by significantly higher degrees of LV dilation and depressed LV ejection fraction. Surgeons in this study, particularly those in Europe, may have chosen to more aggressively treat patients with larger, more poorly functioning ventricles, expressly for the purpose of eliminating the IMR thought to play a role in the ongoing progression of LV failure. Whether this accounts for the improved long-term outcomes in the CABG+MVRep group is unclear, but certainly possible. What about the improved 30-day mortality, which is essentially operative mortality? Could it be that the patients in whom the MR was not repaired had such severe uncorrected MR that the postoperative recovery and immediate survival was adversely affected? Perhaps.

One major limitation is that the true degree of preoperative MR is not known nor controlled for. The study used site-reported and not core laboratory assessments for determining the severity of preoperative MR in 99 centers and 22 countries. If there is one valvular lesion for which qualitative severity is in the eye of the beholder, it is MR (transathoracic versus transeophageal; anesthetized versus awake; afterload-induced versus afterload-reduced). This is a major concern.

Another limitation is the failure to separate patients with moderate and severe MR. The hemodynamic and functional differences are not trivial between these groups, and as such, different surgical strategies are typically used. For moderate MR, surgeons typically choose between repairing versus not repairing the valve, whereas for severe MR, the usual question is not whether or not the MR should be corrected, but rather by what method (ie, repair versus replacement).

Deja and colleagues’13 correctly identify other limitations. First, the decision to perform MVRep was by necessity only considered in patients in the CABG group. Additionally, even within the CABG group, the decision to perform MVRep was not randomized but rather left to the surgeon to decide on at the time of surgery. The authors argue in the discussion that surgeons may have been more reluctant to perform mitral procedures in less healthy patients, citing the higher prevalence of diabetes in the CABG+MVRep group.

If one accepts the study results a priori, then the study hypothesis is supported—failure to adequately address significant MR in patients undergoing CABG in the setting of IMR and severe LV dysfunction may lead to poorer short-term and long-term survival. This is seen most convincingly in the 7 patients with moderate to severe IMR randomized to CABG who died in the first 30 days after surgery; 6 of these were patients who had received CABG alone.

Any meaningful discussion of the impact on survival of MVRep in patients with cardiomyopathy must not ignore the elephant in the room (ie, the issue of repair durability). It is difficult to even theoretically conceive that long-term survival would be enhanced by MVRep if it does not durably repair the target lesion. If durability is indeed the sine qua non for MVRep, the crucial question is which patients will prove to have a lasting repair? In other words, which patients have ventricles so diseased that MVRep will make no impact on the progression of remodeling, which would then lead to MR recurrence? The present study makes no comment on the effect of MVRep on postoperative LV ejection fraction, LV volumes, and most importantly, MR recurrence and its impact on survival.

Increasingly, the evidence is mounting that recurrence of MR occurs in those whose ventricles continue to enlarge and remodel. This is not surprising because there must be some critical time point beyond which eliminating the MR will not help the sick LV recover. Braun and colleagues’14 have shown that MVRep in patients with LV end-diastolic diameters greater than 65 mm is associated with higher rates of recurrent MR. De Bonis and colleagues’15 showed that recurrent MR occurs in parallel with the absence of LV reverse remodeling after MVRep for patients with advanced dilated heart failure.

As such, a greater focus must be placed on optimizing methods to understand and improve the durability of repair. A multipronged approach to this would include such factors as (1) ring type selection (flexible versus rigid, partial versus complete ring), but more importantly, (2) identification of patients in whom annuloplasty alone may not address all the extra-annular geometric factors contributing to IMR in the first place (eg, papillary muscle displacement16 as well as both anterior17 and posterior18 leaflet tethering).

A randomized surgical clinical trial attempting to answer many of these questions is currently occurring. The Cardiac Thoracic Surgical Trials Network (CTSNet), funded by the National Institutes of Health and the Canadian Institutes of Health Research, has completed enrollment in a severe IMR trial in which 250 patients have been randomized to either repair or replacement in severe MR secondary to chronic ischemia. Accrual has recently been completed, and analysis and follow-up are currently occurring. The CTSNet is also currently recruiting patients in a moderate IMR trial in which patients are randomized to either repair or no repair in the setting of moderate MR secondary to chronic ischemia. Durability of repair, reverse remodeling, survival, and symptoms are major study end points. To repair or not to repair? Time will tell.

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Disclosures

None.

References


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